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Handedness and dominant side of symptoms in Parkinson's disease

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Abstract

The aim of this retrospective study was to assess the presence of a possible association between handedness and the side of symptom dominance in 963 patients with Parkinson's disease (PD). In only 287 patients the hand dominance was registered. Out of 254 right-handed patients, 158 (62%) had a right-side dominance of PD symptoms, while 96 patients (38%) had left-lateralized symptom dominance ($p < 0.001$). For the 33 left-handed subjects, 18 (55%) had left- and 15 (45%) had right-sided symptom dominance ($p = 0.602$). Right-handedness thus appeared to be associated with right-sided dominance of PD symptoms, while the group of left-handed patients was too small to draw conclusions from. Possible explanations are discussed.

Introduction

Parkinson's disease (PD) is characterized by asymmetry of symptoms at the onset of disease which is generally maintained during disease progression. Assessment with Positron Emission Tomography (PET) has demonstrated a consistent relation between symptom asymmetry and lateralized cerebral function, in such a way that the dominant side of symptoms significantly correlated with reduced dopamine transporter uptake in the contralateral hemisphere. The cause of symptom lateralization in PD, however, remains to be elucidated [1].

A well-known lateralized function in normal conditions is hand dominance, which is related to asymmetry across brain systems [2]. One might speculate whether such brain asymmetry could provide a clue for a possible explanation for lateralization of PD symptoms. In that case a relation between handedness and such symptom lateralization might be expected. This issue has been addressed in a few previous studies, with varying results. Although these studies generally concerned small groups, a relation between hand dominance was suggested in some studies [3-5] but not in all [6-8]. The aim of the present retrospective study was to identify a possible association of handedness with the side of symptom dominance in PD. Moreover, we looked whether a relation could be found between gait-associated disease characteristics and the side of symptom dominance.

Methods

Study population

PD patients were retrospectively identified from a database of the Movement Disorders unit from the Neurology Department of the University Medical Centre Groningen. This database contained a total of 1120 patients with the diagnosis PD, seen over a period of about 9 years. After assessment of the patient files, 157 patients were excluded for reasons such as uncertainty about the diagnosis PD, adjustment of the diagnosis, too many missing data or bilateral disease onset. A group of 963 subjects thus remained. Approval by the local ethical committee was not required for this study as it concerned retrospective analysis of patient files only.

The dominant side of symptoms was based on documented clinical examination, which remained the same over time. Handedness was defined as the reported hand used for writing. To provide support for the correctness of the documented handedness, handedness was also assessed by phone in a small group of patients. In all these interviewed PD patients, of which 26 were documented right-handed and 4 were documented left-handed, the documented handedness was identical to the handedness assessed by phone. The documented handedness was thus inferred to represent a reliable value.

In addition we investigated whether gait profiles were different, associated with the side of symptom dominance. This assessment was motivated by previous suggestions that freezing of gait was related to asymmetric motor performance, in such a way that

right hemisphere dysfunction might easily cause freezing [9]. The following variables were therefore assessed. The time of onset of PD was defined as the first PD-attributed sign noticed by the patient, a relative or a care provider. Next, we applied similar criteria to determine the intervals between the time of initial complaint and reduced arm swing, the start of bilateral disease and the onset of freezing of gait, respectively. Information on these variables was documented by the treating clinician.

To reduce a selection bias for recording of handedness, we additionally analysed differences between the PD group of known handedness and the PD group of unknown handedness. The parameters for this analysis were sex, age of first symptom, age at diagnosis, disease duration unilateral reduced arm swing, disease duration bilateral involvement and disease duration freezing respectively. No statistically significant difference was found between the groups with known and unknown handedness for these parameters, making a selection bias unlikely.

Statistical analysis

The frequency distribution of the dominant side of symptoms in the right- and left-handed patients was analysed with the Chi-square test, which implied a comparison of this distribution with an equal (chance-based) distribution of left- and right-sided symptoms. Differences between patients with right and left dominant symptoms were analyzed with the t-test for continuous variables. Effect sizes were described by the Cohen's d , calculated by the differences divided with the pooled standard deviation.

Results

The study population consisted of 561 (58.3%) males and 402 (41.7%) females. A total of 503 patients (52%) were characterized by right-sided symptom dominance while in 460 patients (48%) symptoms were dominant on the left side. The handedness was reported to be right-sided in 254 patients (26%) and left-sided in 33 (3.4%), while this parameter was unknown in 676 (70%). Right-handed PD patients had significantly more often symptoms on the right than on the left side ($p < 0.001$) (Table 1). Although left-handed patients showed a small excess of left-dominant symptoms, this result did not reach statistical significance ($p = 0.602$). The distribution of side of symptom dominance in relation to handedness was similar between males and females. We did not find significant associations between gait-associated disease characteristics and the side of symptom dominance (Table 2). Such association was not seen in the group of only right-handed PD patients either.

Discussion

Our results showed a significant excess of right-sided symptom dominance in right-handed patients with PD, while in the smaller group of left-handed patients no significant preference of left-sided symptoms was seen. These results provide support for previous studies that have reported such association [3-5], which remained a conflicting issue in the literature because absence of this association has been published too [6-8]. The small number of left-handed subjects in our study is consistent with the distribution of handedness found in previous PD research [3-4, 7-8] as well as the distribution of about 10% left-handedness in the general population [10]. An ascertainment bias for right-handedness seems therefore unlikely. As our study concerned a retrospective assessment, registration of handedness was according ordinary clinical convention. It appeared that in 30% of the examined PD patient files, handedness was documented. The resulting group of 287 patients can nevertheless be considered as appropriate in size to draw conclusions from. In this respect, it may be relevant to notice that in earlier studies no association was found in groups of, respectively 85, 187 and 472 patients [6-8], while positive associations were found in idiopathic PD populations of 46, 307 and 1277 patients, respectively [3-5]. The different methods that were previously used for assessing handedness might be an additional reason for the above listed differences. Only using recall for determining the side of disease onset, which increases the risk of error, might have been a reason that no association was found in a previously studied group of 472 PD patients [8]. Identifying the onset side by a chart review reduces errors [5-7]. This method is even more robust after excluding patients with a shifted and thus uncertain side of symptom dominance. The latter has been applied in the present study.

A clear explanation for the association between right-handedness and right-sided dominance of PD symptoms has not been given in previous publications. The idea that the association between side of initial symptoms and hand preference might be due to an attention bias for the dominant hand [3] seems not valid because unilateral distribution of symptoms remains during disease progression. As handedness reflects brain asymmetry [2], one wonders whether such asymmetry could be a factor influencing the lateralization of PD symptoms. Is increased movement complexity, enabled by the most skilled hand, a risk factor for dopamine cell loss in the dominant hemisphere? In this respect, an excitotoxic effect of glutaminergic innervation of the substantia nigra might be considered [11]. In animal studies, however, the opposite seemed to be the case: forced exercise might be protective [12]. Asymmetry in PD has been phrased to be a mystery. The association of such asymmetry with right-handedness further adds to this mystery but, on the other hand, provides a challenge to further elaborate on this clue. Prospective research on PD should therefore include quantitative assessment of pre-existing handedness.

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Table 1 – Handedness distribution with symptom dominance in PD

	PD right-sided sympt. dominance	PD left-sided sympt. dominance	Summed number
Right handedness	158 (62%)*	96 (38%)*	254
Left handedness	15 (45%)	18 (55%)	33
Unknown handedness	330 (49%)	346 (51%)	676
All known and unknown handedness	503 (52.2%)	460 (47.8%)	963
Only known handedness	173 (60.3%)	114 (39.7%)	287

The frequency distribution of the dominant side of symptoms in the right- and left-handed patients with Parkinson's disease. * = $P < 0.001$ for difference in the side of symptom dominance in right handed patients (Chi-square test, compared to equal left-right symptom distribution).

sympt. = symptom.

Table 2 – Disease characteristics in relation to side of symptom dominance in PD

Disease characteristics	Right sided	Left sided			
	symptoms	symptoms			
	Mean (SD)	Mean (SD)	Difference	P-value	Effect
	N	N	(95% CI)		size
Age of first symptom (y)	58.3 (12.6)	57.6 (12.3)	-0.773	0.375	-0.062
	437	383	(-2.482–0.936)		
Age at diagnosis (y)	61.8 (11.9)	61.0 (12.2)	-0.742	0.433	-0.062
	334	317	(-2.600–1.116)		
Disease duration unilateral reduced arm swing (y)	3.5 (3.6)	4.1 (4.4)	0.592	0.175	0.15
	204	138	(-0.265–1.450)		
Disease duration bilateral involvement (y)	3.1 (3.6)	3.1 (3.6)	-0.062	0.864	-0.018
	217	171	(-0.778–0.653)		
Disease duration freezing (y)	9.7 (5.6)	10.5 (6.2)	0.771	0.377	0.133
	101	83	(-0.945–2.488)		

A difference of disease characteristics with a positive value indicates a higher value for patients with left compared right sided symptoms. Disease duration concerned the interval between initial complaint and the indicated symptom. N = number, y = year, CI = confidence interval.